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08/[illegible]	[illegible]	CAPUTA, A	

18N1/0815

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EXAMINER	
1813	
ART UNIT	PAPER NUMBER
	31

DATE MAILED:

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

☒ This application has been examined ☒ Responsive to communication filed on 6/30/95 ☒ This action is made final.

A shortened statutory period for response to this action is set to expire 3 month(s), 0 days from the date of this letter.
Failure to respond within the period for response will cause the application to become abandoned. 35 U.S.C. 133

Part I THE FOLLOWING ATTACHMENT(S) ARE PART OF THIS ACTION:

1. ☐ Notice of References Cited by Examiner, PTO-892.
2. ☐ Notice re Patent Drawing, PTO-948.
3. ☐ Notice of Art Cited by Applicant, PTO-1449.
4. ☐ Notice of Informal Patent Application, Form PTO-152.
5. ☐ Information on How to Effect Drawing Changes, PTO-1474.
6. ☐ _____

Part II SUMMARY OF ACTION

1. ☒ Claims 1-3, 10-16 are pending in the application.
   Of the above, claims _____ are withdrawn from consideration.
2. ☒ Claims 4-9, 17-20 have been cancelled.
3. ☐ Claims _____ are allowed.
4. ☒ Claims 1-3, 10-16 are rejected.
5. ☐ Claims _____ are objected to.
8. ☐ Claims _____ are subject to restriction or election requirement.
7. ☐ This application has been filed with informal drawings under 37 C.F.R. 1.85 which are acceptable for examination purposes.
8. ☐ Formal drawings are required in response to this Office action.
9. ☐ The corrected or substitute drawings have been received on _____. Under 37 C.F.R. 1.84 these drawings are ☐ acceptable. ☐ not acceptable (see explanation or Notice re Patent Drawing, PTO-948).
10. ☐ The proposed additional or substitute sheet(s) of drawings, filed on _____ has (have) been ☐ approved by the examiner. ☐ disapproved by the examiner (see explanation).
11. ☐ The proposed drawing correction, filed on _____, has been ☐ approved. ☐ disapproved (see explanation).
12. ☐ Acknowledgment is made of the claim for priority under U.S.C. 119. The certified copy has ☐ been received ☐ not been received ☐ been filed in parent application, serial no. _____; filed on _____
13. ☐ Since this application appears to be in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11; 453 O.G. 213.

[illegible]er

EXA[illegible]CTION

Part III DETAILED ACTION

1. Applicant's Amendment received March 3, 1995 was entered as Paper No. 26. Claims 4-9 and 17-20 have been cancelled. Claims 1-3, and 10-16 are pending. Species No. 27 as set forth on Paper No. 9 mailed August 9, 1993 is examined for prior art.

2. The text of the 35 U.S.C. Code not included in this Office Action can be found in the prior Office Action.

3. The Declaration under 37 C.F.R. 1.132 by Scofield was received April 3, 1995 and entered as Paper No. 27. Said declaration was placed in the application, and considered. However, the declaration does not address any rejection as set forth in the last Office Action.

4. The prior objection to the use of trademarks is withdrawn upon further consideration by the Examiner.

5. The prior objection to the title of the invention is withdrawn in view of applicant's amendment.

6. The prior objection to the specification under 35 U.S.C. § 112, first paragraph for failing to provide an enabling disclosure is maintained.

b. As set forth previously the specification is non-enabled for scope of the elected peptides. Particularly the specification lacks a sufficient disclosure which additions, or deletions to the elected peptide which consist of the recited sequence would have been useful.

Applicant submits the Examiner provides no support for the argument that additions, or deletions to the peptide would not have been expected to be useful. Applicant's arguments are not persuasive. Virji et al. teach peptides of 7 amino acids of an

outer membrane protein did not react with antibodies. Further as presented by applicant in his arguments, hexapeptides of an autoantigen, histidyl tRNA synthase antigen did not react with antibodies (see Paper No. 26, page 10). Since peptides of 6 or 7 amino acids of two distinct proteins do not appear to react with antibodies as set forth in the art it is not predictable to one skilled in the art if peptides of less than the recited sequence (e.g. 7 amino acids or less) would have been useful as claimed.

Furthermore, since additions of amino acids to the peptide would have been expected to alter tertiary structure, and the recognition of antibody to the antigen, it would have been undue experimentation for a skilled artisan in the art to determine which additions to the peptide would not affect the structure and binding of the peptide to the antibody.

Applicant's reference to the teachings of Watson et al., and Eisen et al. are noted. However, the teachings of Watson et al. is not sufficient to overcome the rejection since said reference does not teach peptides of 5 to 8 amino acids bind to antibody as suggested by applicant, only that a peptide comprising a binding site (epitope) of 5 to 8 amino acids is capable of binding antibodies. Since neither the art presented by applicant, nor the specification provide evidence that a peptide consisting of the epitope is capable of binding antibodies, applicant's arguments are not persuasive. The teachings of Eisen et al. is noted. However, the teachings of Eisen et al. are not sufficient to overcome the rejection since Eisen et al. teachings are directed to what conformation the binding region (i.e. epitope) has. Eisen et al. does not provide guidance to what affect the addition or deletions amino acids will have on the epitope. For the reasons set forth above, and in the last Office Action said rejection is maintained.

However, the prior objection to the specification as set forth under sections c) and d) of the last Office Action (see

pages 4-6) is withdrawn in view of applicant's argument and amendment.

7. The prior rejection of claims 1-3, and 10-16 under 35 U.S.C. § 112, first paragraph, is maintained.

8. The prior rejection of claims 1-3, and 10-16 under 35 U.S.C. § 103 as being unpatentable over Deutscher et al., in view of Wotiz et al. (U.S. Patent No. 5,312,752), Voller et al., and Geysen et al., is maintained as set forth in the last Office Action.

Applicant argues that the Examiner is using hindsight to make the prior rejection. Applicant's arguments are not persuasive. Since: 1.) it is known that the 60 kda ribonucleoprotein is useful for diagnosis as set forth by Deutscher et al., 2.) both the ribonucleoprotein and estrogen receptor have a zinc binding motiff which are characterized as having cysteine and histidine residues (see Wotiz et al.-Column 16; lines 55-68 and Column 17, lines 1-8 and Deutscher et al.-Figure 5 and page 9483; Column 1), and 3.) antibodies to the zinc binding motif of the estrogen receptor are specific and do not cross react with other receptors as set forth by Wotiz et al., it is the Examiner's position that it would have been reasonable for one of ordinary skill in the art to expect the zinc binding motif of the 60 kDa ribonucleoprotein would have been useful for diagnosis.

Applicant submits that one of ordinary skill in the art would not have used the zinc region of 60 kDa ribonucleoprotein as set forth by Deutscher et al. since it is different from the zinc binding region of the estrogen receptor. Applicant's argument is noted. However, applicant arguments are not persuasive. Since Wotiz et al. teach antibodies of the zinc binding region of the estrogen receptor do not cross react with

other receptor proteins despite the zinc binding motiff appears to be conserved among various steroid receptors (see Wotiz et al. Column 16; lines 55-68 and Column 17, lines 1-8) it would have been reasonable for one of ordinary skill in the art to expect antibodies of the zinc binding motiff of 60 kDa ribonucleoprotein which contains cysteine and histidine residues as the zinc binding region of the estrogen receptor would have been useful for diagnosis.

Applicant argues: 1.) it is well established that is the secondary and tertiary structures which form the epitopes that are specifically reactive with antibodies, and 2.) it is the tertiary structure of the protein which is the controlling factor which determines the reaction of the protein with antibodies. Applicant's arguments are noted. However, said argument is not persuasive. Since Deutscher et al. teach that autoantibodies are capable of reacting with denatured 60 kDa ribonucleoprotein on a Western blot as exemplified on Figure 3 it would have been reasonable for one of ordinary skill in the art to expected the tertiary structure is not the controlling factor which determine the reaction of the protein with the antibody. Since: 1.) it well known in the art that a number of epitopes (i.e. binding region) are formed by the linear sequence (i.e. see Eisen as submitted by applicant), 2.) it is well known in the art that small synthetic peptide are capable of reacting with antibodies (i.e. see Eisen as submitted by applicant), and 3.) autoantibodies against the 60 kDa ribonucleoprotein are capable of reacting with linear epitopes as exemplified by Deutscher et al. who teaches the denatured 60 kDa ribonucleoprotein is capable of reacting with autoantibodies it is the Examiner' position that it would have been reasonable for one of ordinary skill in the art to expect a peptide of the zinc binding region would have been able to bind antibody.

Applicant argues one of ordinary skill in the art would not use the method of Geysen et al. due to the technical difficulties and lack of reproducibility of said method as evidenced by Miller et al. who teach peptides of 6 amino acids from histidyl tRNA synthase did not bind autoantibodies. Applicant's arguments are not persuasive. It is the Examiner's position that one of ordinary skill in the art would not have been persuaded of evidence by Miller et al. that the method of Geysen et al. lacks reproducibility and has technical difficulties especially since: 1.) the reference by Miller et al. to support applicant's arguments was not provided, 2.) peptides of 7 amino as used by Miller et al. would not have been expected to be useful at the time of the invention in view of the teachings of Virji et al. as set forth above and 3.) Geysen et al. teaching of the preferred use of octapeptides (see page 265) would have been expected to preclude the technical difficulties as set forth by Miller et al. who teach of the inability of antibody to bind peptides of 6 amino acids (see Paper No. 26).

For the reasons set forth above, and in the last Office Action said rejection is maintained.

9. The prior rejection of claims 1-3, and 10-16 under 35 U.S.C. § 112, second paragraph, is maintained.

Since applicant failed to respond for using the phrase "sequence of epitope" and what constitutes as the minimum length of the peptide said rejection is maintained as set forth in the last Office Action.

However, the rejection for use of the term "different" and what constitutes as "autoimmune disorders" is withdrawn in view of applicant's amendment.

10. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. § 1.136(a).

A SHORTENED STATUTORY PERIOD FOR RESPONSE TO THIS FINAL ACTION IS SET TO EXPIRE THREE MONTHS FROM THE DATE OF THIS ACTION. IN THE EVENT A FIRST RESPONSE IS FILED WITHIN TWO MONTHS OF THE MAILING DATE OF THIS FINAL ACTION AND THE ADVISORY ACTION IS NOT MAILED UNTIL AFTER THE END OF THE THREE-MONTH SHORTENED STATUTORY PERIOD, THEN THE SHORTENED STATUTORY PERIOD WILL EXPIRE ON THE DATE THE ADVISORY ACTION IS MAILED, AND ANY EXTENSION FEE PURSUANT TO 37 C.F.R. § 1.136(a) WILL BE CALCULATED FROM THE MAILING DATE OF THE ADVISORY ACTION. IN NO EVENT WILL THE STATUTORY PERIOD FOR RESPONSE EXPIRE LATER THAN SIX MONTHS FROM THE DATE OF THIS FINAL ACTION.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Anthony C. Caputa, whose telephone number is (703)-308-3995. The examiner can be reached on Monday-Thursday from 8:30 AM-6:00 PM. The examiner can be reached on alternate Fridays. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor Ms. Christine Nucker, can be reached at (703)-308-4028

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist, whose telephone number is (703)-308-0196.

Papers related to this application may be submitted to Art Unit 1813 by facsimile transmission. The faxing of such papers must conform with the notice published in the official Gazette 1096 OG 30 (November 15, 1989). The Fax number is (703)-305-7939.

Anthony C. Caputa, Ph.D.
August 9, 1995

MARY E. MOSHER
PRIMARY EXAMINER
GROUP 1800